University Hospitals
Cleveland | Ohio

UH Innovations In Neurosciences

University Hospitals Neurological Institute

New Horizons for Trigeminal Neuralgia

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New Endeavors

To remain at the forefront of innovative research and exceptional patient care, University Hospitals Neurological Institute based at UH Case Medical Center in Cleveland, Ohio, is evolving in vitally important ways.

Since early 2008, we have recruited more than two dozen outstanding physicians. We restructured our institute to create 15 Centers of Excellence to better align the expertise of our professional staff with the unique challenges posed by disorders such as epilepsy, brain tumors, stroke and Alzheimer's disease. We expanded our collaborative efforts with the UH Ireland Cancer Center and UH Rainbow Babies & Children's Hospital, enabling us to team with their specialists to provide personalized, state-of-the-art care for each of our patients. We also continued our focus on developing and testing pioneering treatments through our partnership with Case Western Reserve University School of Medicine.

UH Innovations in Neurosciences is a new, biannual publication designed to inform the medical community of some of the most promising, leading-edge methods of diagnosis and treatment for neurological disorders now available to patients at the UH Neurological Institute. Our neurosurgeons are making great strides in the treatment of trigeminal neuralgia through the application of new imaging technology that enhances the preoperative visualization of the neurovascular anatomy. Physicians at our Stroke and Cerebrovascular Center are enrolling patients in a national multicenter clinical trial comparing aggressive medical therapy alone with medical therapy plus stenting for the prevention of stroke in high-risk patients. Also, last year our Epilepsy Center became the first such center in the U.S. to offer a pioneering surgical technique that preserves memory while controlling seizures originating in the hippocampus.

We invite you to learn more about the UH Neurological Institute, and to partner with us to offer your patients the highest standard of care in a compassionate, patient-focused environment.

Sincerely,

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University Hospitals Case Medical Center
The Harvey Huntington Brown Jr. Professor and Chair,
Department of Neurological Surgery
Case Western Reserve University School of Medicine

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UH Innovations in Neurosciences
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Among the nation's leading academic medical centers, University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine. The Case Western Reserve University School of Medicine is a nationally recognized leader in medical research and education.

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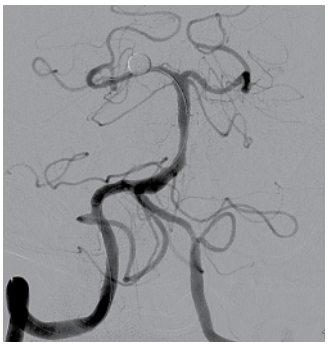
CASE WESTERN RESERVE UNIVERSITY
SCHOOL OF MEDICINE

The commitment to exceptional patient care begins with revolutionary discovery. Faculty at the Case Western Reserve University School of Medicine, who also are physicians at UH Case Medical Center, are at the forefront of medical research and innovation. The School of Medicine is the largest medical research institution in Ohio and among the nation's top medical schools for research funding from the National Institutes of Health.

Among the nation's leading academic medical centers, University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine. The Case Western Reserve University School of Medicine is a nationally recognized leader in medical research and education.

Finding New Answers

A new study at UH targets high-risk stroke patients



Severe stenosis of the basilar artery successfully treated with stenting

Cathy Sila, MD, is on the Board of Directors of the Intersocietal Accreditation Commission to develop credentialing for Carotid Stenting Facilities.

The risk of recurrent stroke is especially high among patients with symptomatic stenosis of a major intracranial artery, a condition that accounts for an estimated 70,000 to 90,000 strokes or transient ischemic attacks (TIAs) per year in the United States.

In an effort to identify more effective treatment options for these patients, Neurological Institute physicians at University Hospitals Case Medical Center are participating in a national multicenter research trial that utilizes aggressive medical therapy, including careful management of the patients' blood pressure, cholesterol and other key risk factors, as well as placement of a stent to widen the stenotic artery. The Stenting vs. Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial, funded by the National Institutes of Health (NIH) to Case Western Reserve University School of Medicine, builds on previous research that changed the conventional wisdom about appropriate medical therapy for intracranial arterial stenosis.

"We learned from previous NIH-funded trials that aspirin is a safer and equally effective alternative to warfarin in preventing recurrent stroke," says **Cathy Sila, MD**, Director, UH Neurological Institute Stroke and Cerebrovascular Center, holder of the George M. Humphrey II Chair in Neurology, and Professor, Neurology, Case Western Reserve University School of Medicine. "We also found that patients with lower blood pressures did better, busting another commonly held wisdom that higher blood pressures would be more likely to improve blood flow to the brain.

"We identified a subgroup, those patients with severe blockage in the basilar artery, as having a 22 percent risk of another stroke within one year."

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>
> *– Cathy Sila, MD*

TO STENT OR NOT

In the meantime, re-engineering of coronary stents has yielded devices suitable for the thinner, more twisted arteries of the brain. "Now is the time to compare whether adding the stent on top of a very aggressive medical program is better at preventing stroke than an aggressive medical program alone for this very high-risk subgroup."

All patients enrolled in the SAMMPRIS trial receive aspirin and clopidogrel and other medications to control their hypertension, cholesterol and diabetes, and most medications are free of charge. In addition, a "life coach" helps participants quit smoking, exercise, lose weight and manage their stress.

VERY PRELIMINARY RESULTS

According to Dr. Sila, the two UH patients enrolled in the study to date are doing well. "Our first patient was started on the aggressive medical regimen as soon as we confirmed that his stenosis was more than 70 percent blocked, severe enough to be appropriate for this trial. His TIA symptoms improved without any noticeable difference on his angiogram. Then, after receiving the stent, he had one slight episode and his symptoms have not recurred since. The second patient was randomized to the medical treatment alone, and he's responding well, too."

Dr. Sila says she expects the trial will take four or five years to complete. "It's wonderful to be able to offer such a comprehensive treatment program for patients at such high risk for stroke."

Robert Tarr, MD, Associate Director, UH Neurological Institute, Division Chief of MRI/Neuroradiology, and Professor, Case Western Reserve University School of Medicine, is a co-principal investigator for the SAMMPRIS trial and performed the stent placement in the first patient.

Enroll Your Patients

To find out if one of your patients qualifies for this study, call **216-844-2724**.

A Heartbreaking Disease Meets Its Match

Improving treatment for trigeminal neuralgia

Jonathan Miller, MD, is the winner of 12 national neurosurgical awards, including the 2008 Young Clinician Investigator Award from the American Association of Neurological Surgeons.

The searing pain of trigeminal neuralgia (TN), also known as tic douloureux, afflicts an estimated one in 15,000 people, most of them over the age of 50. Although TN is a relatively rare syndrome, its symptoms are devastating.

At University Hospitals Case Medical Center, a pioneering neuroimaging technique is helping neurosurgeons determine the optimal treatment of patients with TN. Concurrently, research spearheaded by **Jonathan Miller, MD**, Director, Functional and Restorative Neurosurgery, University Hospitals Case Medical Center, and Assistant Professor, Neurological Surgery, Case Western Reserve University School of Medicine, has led to advances in the classification and surgical treatment of TN.

CURRENT TN TREATMENTS

A disorder of the fifth cranial (trigeminal) nerve, TN is characterized by the sudden onset of lancinating, shock-like pain on one side of the face. The most common cause is vascular compression at the trigeminal nerve root entry zone in the cerebellopontine angle (CPA), says Dr. Miller, as documented in his April 2009 article for the *Journal of Neurosurgery,* 110(4):627-32. Pain can be triggered by stimuli such as shaving, brushing teeth or even a light breeze. According to Dr. Miller, the first line of treatment is usually an antiepileptic drug such as carbamazepine or gabapentin.

While about 40 percent of patients achieve long-term relief with medical therapy, most experience little or no pain relief, or their symptoms recur. These patients become candidates for surgical intervention, Dr. Miller says.

"Sometimes physicians wait too long before referring a patient for surgery; they see it as a last resort, and keep trying different medications," he says. "But with TN, once a patient has failed one medication, the chance that a different medication or combination of medications is going to work is low. That's an indication that physicians should proceed to more aggressive therapy initially."

BETTER THAN SURGERY

Surgical interventions can include a variety of lesioning procedures, such as radiofrequency thermocoagulation, glycerol injection or balloon compression. These procedures, performed under local anesthesia, involve percutaneous access and precise damage to the trigeminal ganglion. While they offer relief to some patients, the procedure that yields the best chance of long-term freedom from pain is microvascular decompression (MVD). "This technique was pioneered in the 1970s. The literature shows, and our own research confirms, that more than 70 percent of patients who undergo MVD are pain-free and off medications for 10 years or more. For the vast majority, their pain is gone immediately postoperatively."

Performed under general anesthesia, MVD involves separation or removal of the blood vessels exerting pressure on the trigeminal nerve. Although MVD is more invasive than the lesioning procedures, Dr. Miller points out that because of advanced intraoperative monitoring techniques, complications are rare.

Planning and patient selection for all surgical procedures for TN has been enhanced by a new strategy for the preoperative visualization of the neurovascular anatomy. This approach, developed by Dr. Miller and his colleagues and employed in the Midwest exclusively at University Hospitals, fuses two imaging technologies: 3-D visualization of solid structures by balanced fast-field echo and

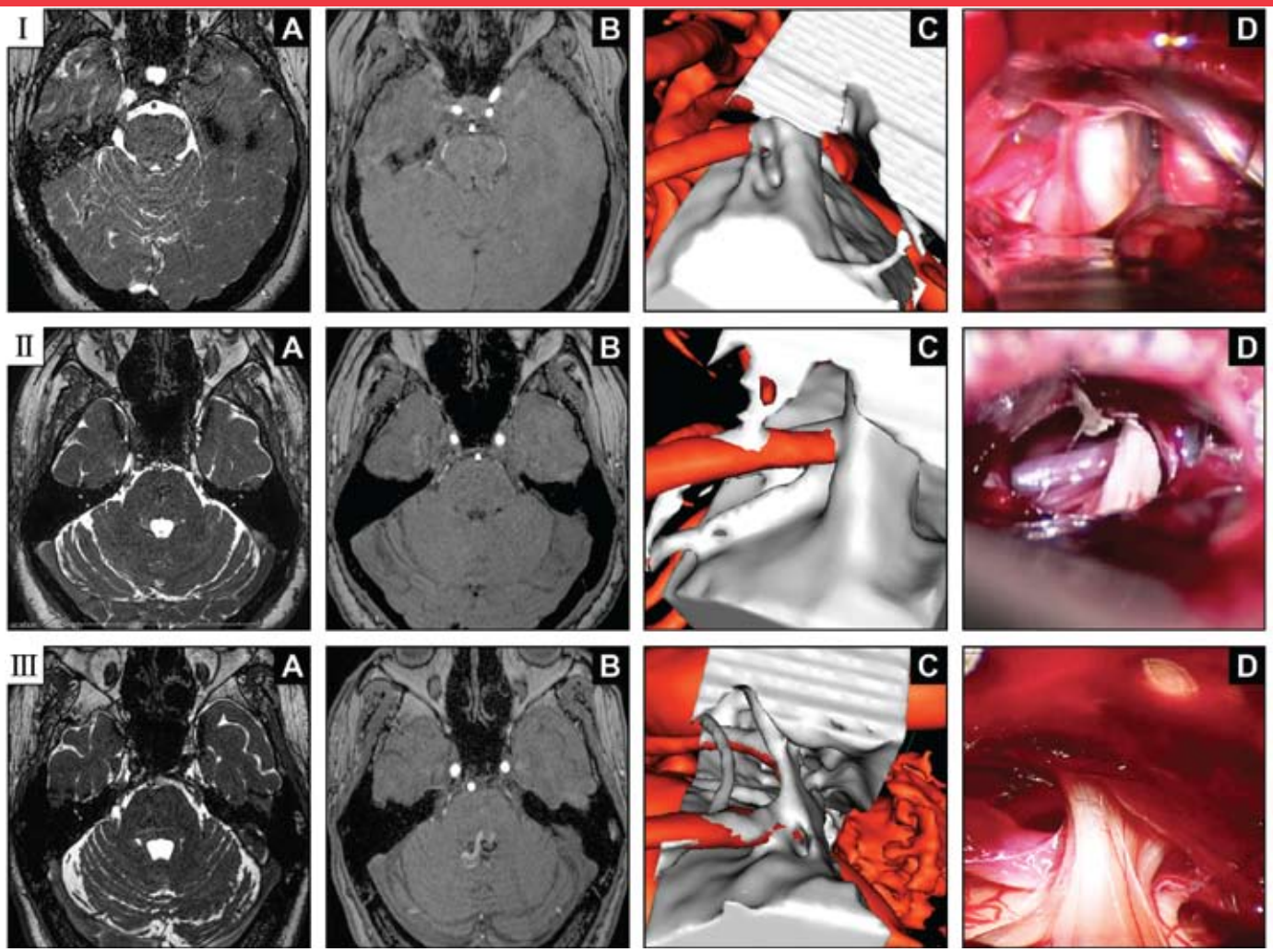
Treatment through the Centuries

The celebrated Greek physician Aretaeus of Cappadocia, who in the second century described a host of diseases including diphtheria, tetanus, asthma and epilepsy, may have provided the first account of trigeminal neuralgia (TN), according to *Neurosurgical Focus*, 18(5):E4, 2005.

In the ensuing centuries, physicians employed a variety of techniques in largely unsuccessful attempts to relieve their patients' excruciating pain. These early treatment methods included tooth extraction, hot baths, wine, the bark of the cinchona tree (which contains quinine), ether, opium and arsenic in gruel.

Pioneering surgeons of the late 19th century laid the foundations of the successful surgical treatment of TN.

"In 1899, Harvey Cushing developed a subtemporal approach that allowed removal of the trigeminal ganglion with minimal retraction of the temporal lobe," says Jonathan Miller, MD. "He called it a gasserian ganglionectomy, and that's really what started Cushing's career as a brain surgeon. It's interesting that a treatment for trigeminal neuralgia sort of started modern neurosurgery. We don't resect the nerve anymore because of the risks associated with postoperative numbness, but it's definitely of tremendous historical importance."



"Images obtained prior to an operation to decompress the trigeminal nerve (A-B) allow for simulation of the interoperative view (C) that closely matches what is seen at surgery (D). In these images, white indicates neural anatomy and red indicates arterial structures. This novel technique allows the surgeon to see the trigeminal nerve and its surrounding structures before the operation, and this can help with patient selection and surgical planning." Reprinted from the *Journal of Neurosurgery* 108:477-482, 2008, cover article.

demonstration of vascular structures by magnetic resonance (MR) angiography and enhanced MR imaging. Described in the *Journal of Neurosurgery*, 108:477-482, 2008, the technique enables UH physicians to visualize the nerves, arteries and veins of the CPA with an unprecedented level of anatomic detail.

A NEW APPROACH TO TN CLASSIFICATION

Patients with TN present with a broad spectrum of symptoms. While most display compression of the trigeminal nerve at surgery, some do not. Patients also vary in their response to surgical treatment, with some showing immediate and long-term improvement following MVD and others suffering a recurrence of symptoms after an initial good result.

Dr. Miller and his team developed a novel system of TN classification based on the preponderance of episodes of lancinating, electric shock-like pain (Type I) versus a more constant aching, throbbing or burning pain (Type II). A study published in the *Journal of Neurosurgery*, 110:620-626, 2009, as well as Dr. Miller's own as referenced earlier in this article, demonstrated that these clinical subtypes are predictive of neurovascular pathology found at surgery (with Type I patients more likely to display arterial compression) and postoperative prognosis.

"We compared our patients who do well after MVD with those who don't, and found that the one factor that made a tremendous difference was whether or not the patient had constant facial pain in addition to the lancinating pain," Dr. Miller says. "If the background pain is more than half your pain, you're Type II; only 30 percent of those patients are pain-free long-term without medication, though 60 percent show some improvement.

"The good news," he says, "is that most people still do get better. From my point of view, MVD is one of the spectacular success stories in clinical surgery. These patients come in horribly disabled and they leave with a long-term cure and no other lasting effects. That's really an amazing result."

A TN Source

Call **216-844-1001** for expert input concerning trigeminal neuralgia. This advice line provides decision-making assistance to other physicians.

Focus on the Hippocampus

UH neurosurgeons break new ground in epilepsy surgery

Hans O. Lüders, MD, PhD, is a fellow of the American Academy of Neurology and editor of the *Textbook of Epilepsy Surgery* (Informa Healthcare 2008).

Epilepsy and seizures affect more than 3 million Americans, and 10 percent of the population will experience a seizure in their lifetime. Antiepileptic drugs control seizures in only about half of all patients with epilepsy; those who fail medical therapy may become candidates for surgery.

A groundbreaking surgical approach to epilepsy treatment, now available at University Hospitals Case Medical Center, is showing promise for a select group of patients whose seizures originate in the hippocampus.

Robert Maciunas, MD, Vice Chairman, Neurosurgery, UH Neurological Institute, and Professor, Neurosurgery, Case Western Reserve University School of Medicine, was the first to perform the procedure, multiple hippocampal transection (MHT), in the United States. After observing Hiroyuki Shimizu, the Tokyo neurosurgeon who developed the technique, Dr. Maciunas began performing the surgery on UH patients in 2008.

PROTECTING MEMORY

"The goal of this surgery is to eliminate epilepsy while preserving memory, which is located in the hippocampus," says **Hans O. Lüders, MD, PhD,** Director, UH Neurological Institute Epilepsy Center, and Professor, Neurology, Case Western Reserve University School of Medicine.

"Resection of the hippocampus is usually effective in controlling seizures, but it causes loss of verbal memory. Instead of removing the hippocampus, MHT is a technique in which small cuts are made slicing the hippocampus. This eliminates epileptic seizures but preserves memory function."

BASED ON NOVEL TECHNIQUES

The concept underlying MHT is similar to that of another method of epilepsy surgery, multiple subpial transection. Using intraoperative electrocorticography to pinpoint the areas of epileptic discharges, the surgeon attempts to interrupt interneuronal connections while preserving vertical projection fibers, which are critical to cortical functions.

"Dr. Maciunas has used this technique with three patients so far, and the results have been very good," Dr. Lüders says.

"None [of these patients] has suffered memory loss. Two are totally free of seizures, and one who had seizures shortly after the surgery no longer has them." (See page 7 for a case study on MHT.)

Milestones in Epilepsy Treatment

1870: John Hughlings Jackson describes and classifies focal epilepsy as a condition in which focal areas of the brain discharge excessively.
1879: Scottish neurosurgeon William Macewen becomes the first to successfully remove an epileptogenic brain tumor.
1893: Fedor Krause becomes the first surgeon to perform intraoperative electrical stimulation of the cerebral cortex.
1912: Phenobarbital, the oldest antiepileptic drug (AED) in common use, is marketed under the name of Luminal.
1939: Testing of phenytoin in an animal model leads to the introduction of a new nonsedating antiepileptic drug.
1963: Sodium valproate's anticonvulsant property is recognized.
1997-2000: Six additional AEDs receive FDA approval.

Candidates for MHT have failed medical therapy, have focal epilepsy coming from the dominant left or right hippocampus, have good memory, and are free of hippocampal atrophy.

"This can only be done by a specialist at an epilepsy center because you are only going to get good results if you select patients appropriately," he says. "We are being cautious and going very slowly, but so far it looks good."

Advances in Epilepsy Surgery Show Promise

Multiple hippocampal transection ends seizures while minimizing memory loss

The University Hospitals Case Medical Center neurological team has helped develop a procedure that minimizes memory loss during epilepsy surgery.

A 38-year-old, right-handed woman presented with a history of recurrent seizures. The first, a dialeptic seizure, occurred in June 2001 and was complicated by pulmonary edema and admission to the intensive care unit. Her husband described this initial occurrence as a behavioral arrest and staring, followed by a fall and loss of consciousness.

A few weeks later, the patient began having recurrent seizures. She reported a 10- to 15-minute "aura" characterized by a "nervous sensation" in her chest, followed by staring, loss of awareness and speech arrest. Afterward, she was unable to speak for up to 15 minutes. Some of the seizures evolved into left-face twitching and generalized tonic-clonic seizures. She was experiencing one to two partial seizures per week, up to a maximum of six partial seizures per day. Her last generalized tonic-clonic seizure occurred two and a half years earlier.

Her past antiepileptic medications included levetiracetam, phenytoin, tiagabine and zonisamide. Currently, she is taking carbamazepine and lamotrigine to control her seizures.

EVALUATION

With the patient cared for by **Hans O. Lüders, MD, PhD**, Director, UH Neurological Institute Epilepsy Center, and Professor, Neurology, Case Western Reserve University School of Medicine, a video/EEG conducted in 2006 documented a secondarily generalized tonic-clonic seizure arising from the right temporal lobe. MRI studies showed no lesion. Additional video/EEGs using depth electrodes supported a diagnosis of right temporal epilepsy.

Testing for temporal functioning, including verbal and visual memory, showed the patient to be in the normal range. A Wada test demonstrated that her right hemisphere was dominant for language. This was an unusual finding, as about 90 percent of the population is estimated to have left-hemisphere dominance for language.

TREATMENT

A multiple hippocampal transection (MHT) was performed on the right hippocampus. The procedure involved the application of six electrodes to the amygdala, the hippocampal head and the posterior part of the hippocampus to record electrocorticography over these areas.

Transections were made between the electrodes, with intraoperative EEGs recording spike discharges along the hippocampus before and after MHT. The EEG readings demonstrated a sharp drop in the number and frequency of spikes after MHT. Abnormal activity – spikes with an amplitude greater than 800 microvolts – decreased from more than 40 spikes per minute before to fewer than five spikes per minute after the MHT had been completed.

OUTCOME

The patient has experienced no seizures in a year and a half since the surgery. At six-months postsurgery, she complained of mild memory deficits. A test of temporal functioning showed a 10 percent drop in immediate recall, which would translate to difficulty remembering names or people she recently met. Memory tests showed no significant change in visual memory. However, additional testing performed at one-year postsurgery indicated that the patient's memory had returned to presurgical levels.

DISCUSSION

Epilepsy emanates frequently from the hippocampus, an area crucial to forming new memories. Although destruction or removal of the hippocampus is effective in treating epilepsy, the result for the patient may very well be deficit of memory. In appropriately selected patients, the MHT procedure can eliminate epilepsy while preserving memory.

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